

THE BIOLOGICAL SYNTHESIS OF CERTAIN
AMINO ACIDS DURING GROWTH

BY

RUTH ELIZABETH LESLIE

B.A., University of Texas, 1932

M.A., University of Texas, 1934

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN
CHEMISTRY IN THE GRADUATE SCHOOL OF
THE UNIVERSITY OF ILLINOIS, 1940

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PART I

THE REPLACEMENT OF PHENYLALANINE AND TYROSINE BY DIIODOTYROSINE

INTRODUCTION

It has been shown by Womack and Rose ^{1,2} that phenylalanine is an indispensable component of the diet, whereas tyrosine is nonessential, but that a sub-optimal level of the former may be supplemented by adequate quantities of the dispensable compound. Because diiodotyrosine is present in the thyroid, it was of interest to determine by feeding experiments whether it might be reduced to tyrosine or phenylalanine to meet the demands of growth. Two experiments were carried out: (a) the substitution of diiodotyrosine for phenylalanine in the absence of tyrosine; (b) the substitution of diiodotyrosine for tyrosine when phenylalanine was supplied at a sub-optimal level.

EXPERIMENTAL

Young albino rats were given a diet containing adequate amounts of fats, carbohydrates, minerals, and vitamins. The protein requirement was met with mixtures of pure amino acids. Diiodotyrosine was prepared according to the method of Wheeler and Jamieson³ by the iodination of tyrosine, and was fed at a level equivalent to the phenylalanine or tyrosine for which it was substituted. In the first experiment the controls receiving 1.2 per cent of phenylalanine gained an average of 42.5 gm. The animals fed an equivalent quantity of diiodotyrosine showed an average loss of 14 gm. over the twenty-eight day experiment. In the second experiment the positive control group, which received 0.4 per cent of phenylalanine supplemented by 0.8 per cent of tyrosine, gained an average of 37 gm. The group which received 0.4 per cent of phenylalanine unsupplemented by tyrosine gained an average of 11.3 gm. Those animals in whose ration 0.4 per cent of phenylalanine was supplemented by 1.91 per cent of diiodotyrosine showed an average gain of 11.6 gm.

SUMMARY

Growth experiments have shown that diiodotyrosine cannot replace phenylalanine; nor can it perform the functions of tyrosine when the latter is used to supplement a sub-optimal level of phenylalanine.

BIBLIOGRAPHY

¹ Womack, M., and Rose, W. C., J. Biol. Chem., **116**, 381 (1936).

² Womack, M., and Rose, W. C., unpublished data.

³ Wheeler, H. L., and Jamieson, G. S., Amer. Chem. J., **33**, 365 (1905).

PART II

THE REPLACEMENT OF LEUCINE BY α -KETOISOCAPROIC ACID AND α -HYDROXYISOCAPROIC ACID

INTRODUCTION

It is of interest whether or not compounds closely related to an indispensable amino acid can replace it for purposes of growth. Investigations of this nature have been conducted in various instances with the unnatural optical isomers, N-acyl and N-alkyl derivatives, esters, the corresponding fatty, keto, hydroxy, and unsaturated acids. In the present study growth experiments were conducted with the α -keto and α -hydroxy acids corresponding to leucine.

EXPERIMENTAL

The feeding test with each compound was carried out on a litter of young albino rats. As controls in each litter two rats received dl-leucine, and two rats received neither leucine nor the compound being studied. In one litter the test group were fed sodium α -ketoisocaproate at a level of 2.78 per cent; in the second litter an equivalent quantity (2.82 per cent) of the sodium α -hydroxyisocaproate was supplied. Otherwise the diets were identical and adequate. A mixture of pure amino acids supplied the required nitrogen and furnished the indispensable amino acids except leucine. The deficient controls lost an average of 12 gm. in both cases; the leucine controls gained an average of

44 gm. The animals receiving the α -keto acid gained from 36 to 46 gm. The animals receiving the α -hydroxy acid gained from 34 to 38 gm.

SUMMARY

Growth experiments have shown that α -ketoisocaproic acid and α -hydroxyisocaproic acid are effective substitutes for leucine, although both are apparently less readily utilized than the natural compound.

PART III

THE REPLACEMENT OF l(+)-ISOLEUCINE BY d(-)-ISOLEUCINE

INTRODUCTION

Both optical isomers of histidine,¹ methionine,² phenylalanine,³ and tryptophane⁴ have been found to be utilized by the rat. The unnatural isomer of arginine has not been tested; but only the natural forms of lysine,⁵ leucine,⁶ valine,⁷ and threonine⁸ support growth. In the present investigation d(-) and l(+) isoleucine were obtained by the resolution of the synthetic racemic compound and were studied in feeding tests to determine their relative availability to the rat for purposes of growth.

EXPERIMENTAL

Synthetic dl-isoleucine was formylated and resolved through the brucine salts into its two enantiomorphs. A litter of young albino rats was divided into three groups, one of which was the negative control and which received neither isomer. Another group was fed l(+)-isoleucine. To the third was supplied d(-)-isoleucine, the unnatural form. In other respects the diets were identical and adequate. In comparison with an average gain of 42 gm. by the animals receiving l(+)-isoleucine and an average loss of 18.5 gm. by the isoleucine deficient controls, the average loss by the animals fed d(-)-isoleucine was 21 gm.

SUMMARY

Feeding experiments have demonstrated that d(—)isoleucine, the unnatural optical isomer, is not utilized by the rat for purposes of growth.

BIBLIOGRAPHY

- ¹ Cox, G. J., and Berg, C. P., J. Biol. Chem., **107**, 498 (1934).
- ² Jackson, R. W., and Block, R. J., Proc. Soc. Exper. Biol. and Med., **30**, 587 (1932-1933).
- ³ Womack, M., and Rose, W. C., unpublished data.
- ⁴ Berg, C. P., and Potgieter, M., J. Biol. Chem., **94**, 661 (1932).
- ⁵ Berg, C. P., J. Nutrition, **12**, 617 (1936).
- ⁶ Fierke, S. S., and Rose, W. C., unpublished data.
- ⁷ Eppstein, S. H., and Rose, W. C., unpublished data.
- ⁸ West, H. D., and Carter, H. E., J. Biol. Chem., **122**, 611 (1939).

VITA

The author was born April 26, 1911, in Bonham, Texas. She attended to Duncan Ward School and was graduated from Bonham High School in June 1928. In July 1928 she was awarded one of the six national Francis P. Garvan Scholarships by the Prize Essay Committee of the American Chemical Society for her essay, "The Relation of Chemistry to the Enrichment of Life." She received the B.A. degree with highest honors from the University of Texas in June 1932 and the M.A. degree in August 1934. She served at the University of Texas as tutor in inorganic and organic chemistry, and from 1934 to 1936 was part-time instructor in organic and physiological chemistry. In 1936-1937 she taught in the public school system of Bonham, Texas. At the University of Illinois she has been assistant in biochemistry, and for the last year has been the recipient of a graduate fellowship.

